RESPONSE TO OFFICE ACTION

A. Status of the Claims

Claims 1, 2 and 4-10, 25, 33, 35, 39, 42 and 43 are currently pending. Claims 25, 33, 35, 39, 42 and 43 are withdrawn and claims 1,2 and 4-10 are under consideration in the case and are presented herein for reconsideration.

B. Rejections Under 35 U.S.C. §103(a)

The Action rejects claims 1, 2, and 4-10 under 35 U.S.C. § 103(a) as being unpatentable over Barry *et al.* (U.S. Patent No. 5,463,175) in view of Strauch *et al.* (U.S. Patent No. 5,276,268) and Kishore *et al.* (U.S. Patent 5,312,910) and in further view of Shah *et al.* (U.S. Patent No. 5,188,642). The Action asserts that "Barry *et al.* teach introducing a transgene encoding the glyphosate tolerant GOX (glyphosate oxidase) and a transgene encoding a sulfonylurea-resistant form of the maize acetolactate synthase gene (ALS) into a corn cell" but do not teach introducing a glyphosate tolerance gene and an ALS transgene into a soybean, or a plant with a phosphinothricin (PTC)-resistance gene. The Action further asserts that Strauch *et al.* teach incorporating a PTC gene into a plant to render it resistant to glufosinate, Shah *et al.* teach an EPSPS enzyme resistant to glyphosate and a soybean transformed therewith, and Kishore *et al.* teach a transgene encoding an EPSPS enzyme resistant to glyphosate and methods of using a plant (including soybean) transformed therewith to control weeds in a field. The Action asserts that this combination of teachings makes the claimed invention obvious. Applicants respectfully traverse.

1. The Combination of References Does Not Teach Or Suggest the Claimed Invention

The current rejection cites Barry *et al.* for disclosing introducing a transgene encoding glyphosate oxidase (GOX) and a transgene encoding a sulfonylurea-resistant form of the maize acetolactate synthase gene (ALS) into Black Mexican Sweet (BMS) corn cells (Barry *et al.*, Ex. 5 at col. 37, line 50-col. 38, line 51). That disclosure is cited in the Action as providing a rationale for combining glyphosate resistance and sulfonylurea resistance in a soybean plant, making it ". . . *prima facie* obvious . . . to modify the teachings of Barry *et al.* to use the glyphosate tolerant EPSPS transgene of Shah *et al* combined with a herbicide tolerant PCT transgene of Strauch *et al.* to transform soybean plants." Page 3 of the Action. However, the skilled artisan would not read Barry *et al.* as teaching that two herbicide resistance genes could or should be combined into a soybean plant to yield tolerance to both herbicides or that any benefit would be obtained therefrom.

The cited columns 37 and 38 (Example 5) of Barry *et al.* refer to the introduction of a GOX gene into Black Mexican Sweet (BMS) corn cells. The plasmid having the GOX gene, pMON19632, ". . . was introduced into BMS corn cells by co-bombardment with EC9, a plasmid containing a sulfonylurea-resistant form of the maize acetolactate synthase gene. . . . Transformants were selected on MS medium containing 20 ppb chlorsulfuron. After initial selection on chlorsulfuron, the calli was assayed by glyphosate oxidoreductase Western blot." Barry *et al.* , col. 38, lines 2-11. Plasmid EC9 is further described in U.S. Patent No. 5,593,874, at FIG. 19 (showing a map of EC9) and Example 3, at cols. 13-14. In that example, BMS corn cells were also bombarded with EC9 and a test plasmid:

> EC9 (FIG. 19), a plasmid containing an acetolactate synthase gene, ***was included for use in chlorsulfuron selection for transformed control cells***. A second plasmid containing the test construct was co-precipitated with EC9.

U.S. Patent No. 5,593,874, col. 13, line 67 - col. 14 line 4 (emphasis added). Barry *et al.* therefore do not teach or suggest any benefit to the resistant ALS gene in the plant cells other than as a ***selectable marker***, *i.e.*, to identify transformed cells in tissue culture. A further examination of Example 5 of Barry *et al.* also confirms that any use of resistance to sulfonylureas was contemplated only for selection of *in vitro* cells co-transformed with a different gene of interest, since only GOX levels were evaluated, and there was no suggestion that EC9 was useful for anything other than *in vitro* experiments.

Applicants additionally provide herewith as **Exhibit A** the Declaration of Dr. Paul Feng under 37 C.F.R. §1.132 further establishing, at Paragraph 6, that Barry *et al.* would not teach or suggest stacking herbicide resistance genes in whole plants, for the reasons discussed above. Dr. Feng further points out that the BMS cells used in the experiments described in Example 5 of Barry *et al.* are not regenerable into whole plants, which also points against Barry *et al.* suggesting whole plants resistant to two herbicides.

In light of the above discussion, it is clear that Barry *et al.* do not teach or suggest the stacking of a sulfonylurea-resistant ALS gene with a glyphosate resistance gene to create the claimed plants and seeds. Additionally, neither Strauch *et al.*, Kishore *et al.*, or Shah *et al.*, alone or in combination, provide such a teaching or suggestion. Since there is no such teaching or suggestion, Applicants respectfully assert that the current rejection under 35 U.S.C. 103(a) should be withdrawn.

2. No Reasonable Expectation of Success Was Present at the Priority Date

As noted previously, there was no reasonable expectation of a benefit or success generally regarding production of a soybean plant displaying resistance to two herbicides at the priority date of the present application over Barry *et al.*, Strauch *et al.*, Kishore *et al.*, and Shah *et al.*

In that regard, Applicants point out that Barry *et al.* used a maize sulfonylurea-resistant ALS gene to transfect non-regenerable corn cells. That would in no way lead the skilled artisan to believe that a maize sulfonylurea-resistant ALS gene would make soybeans resistant, particularly when in combination with a second herbicide tolerance transgene.

Exhibit A, the Declaration of Dr. Paul Feng under 37 C.F.R. §1.132, additionally provides a summary of experiments establishing that the stacking of two glyphosate resistance genes, GOX and CP4, did not lead to increased glyphosate resistance in corn, tobacco and cotton, contrary to what would be predicted. This further establishes that stacking of herbicide resistance traits is not *a priori* predictable as is assumed in the Action, and that there would not have been any reasonable expectation that a benefit would be obtained by stacking a transgene conferring resistance to glyphosate herbicide and a transgene conferring resistance to glufosinate herbicides in a soybean.

Applicants further again call attention to the Declaration of Dr. Byrum provided with of the Response dated October 16, 2006 of the instant application. That Declaration points out that the present disclosure describes the first soybean plant that has more than one herbicide resistance transgene. As explained therein, additional uncertainty of any benefit from stacking the specified herbicide tolerance traits came from the fact that expression of herbicide resistance transgenes requires manipulation of complex metabolic pathways in plant cells, including in numerous diverse tissues found throughout the plant, and expression of enzymes not normally

present in a plant creates a "metabolic drag" reducing energy by diverting resources to the expression of a transgene(s), combined with the uncertainty of potential interactions among inter-related metabolic pathways. For example, Dr. Byrum has explained that that "[h]erbicide resistance traits add the uncertainty of potential interactions among interrelated metabolic pathways, including negative or positive feedback regulation of different pathways from altered substrate or precursor production." Declaration of Dr. Joseph R. Byrum Under 37 C.F.R. §1.132, submitted in the instant application on June 1, 2004, at page 3.

Applicants also reiterate that mixtures of herbicides are not predictable in the amount of damage they cause in relation to each herbicide alone, as illustrated in U.S. Patent 5,599,769 (Hacker *et al.*), teaching that combinations of glyphosate or glufosinate with a sulfonylurea herbicide are synergistic. That uncertainty would have further added to the unpredictability of the resistance of the claimed soybean to tolerate both glyphosate and a glufosinate as of the filing date of the parent case.

3. Contemporaneous Studies Regarding the Yield of Herbicide Resistant Crop Plants Teach Away from the Invention

One of skill in the art would have been aware as of the filing date of numerous studies asserting that the presence of a glyphosate tolerance gene resulted in yield suppression in soybeans, compared to varieties lacking a glyphosate tolerance transgene. One of skill in the art would have therefore been taught away from attempting to combine a glyphosate tolerance transgene with a gene conferring sulfonylurea tolerance given the potential impact on yield and the great importance of yield in soybeans. See specification at page 9, para. 43. Examples of these studies are described in two references provided with the Declaration of Dr. Byrum in the Response dated October 16, 2006 of the instant application. Specifically, Raymer and Grey,

Crop Science 43:1584-1589 (2003), at pages 1585-1586, summarize data from field trials from 1995-1996 showing an apparent reduction in yield when glyphosate-tolerant soybean lines were compared with comparable conventional varieties. Additionally, Marking, *Corn and Soybean Digest* March 15, 1999, discusses several studies dating from 1996 that find a "yield lag" due to the glyphosate resistance trait. Marking concludes, "[t]his yield lag factor for RR soybeans has been mentioned by many scientists and top-end growers who made side-by-side comparisons since 1996. . . ." Marking, third paragraph from the bottom. When the studies discussed above showing reduced yield in glyphosate-tolerant soybean varieties are taken into consideration, the skilled artisan at the time of filing would believe that there was a strong likelihood that a herbicide resistance gene leads to a reduction in yield. The skilled artisan would have reasoned that, if one herbicide resistance gene causes a reduction in yield, then stacking two herbicide resistance genes in one plant would likely lead to an intolerable reduction in yield. This teaches away from the present invention by indicating that a plant with more than one herbicide resistance gene would have an unacceptable yield.

4. Conclusion: The Claims Are Not Obvious In Light of the Cited References

To summarize the above discussion, Barry *et al.* does not teach or suggest the claimed invention because Barry *et al.* does not teach or suggest using the herbicide-resistant ALS gene to create a transgenic plant resistant to sulfonylurea herbicides. Additionally, there would not have been a reasonable expectation of success at the time of filing because of uncertainty regarding the suitability and yield of the claimed plant both when untreated and treated with glyphosate and a glufosinate. Further, the prior art taught away from the present invention by indicating that there is a likelihood of a reduced yield with a single herbicide resistance gene, and therefore stacking

two such genes in a single plant would have been expected to reduce yield even further, while it is widely accepted that high yield is the single most important trait in soybeans.

Applicants further submit that the cited Strauch *et al.*, Kishore *et al.*, and Shah *et al.* references do not cure the defect of Barry ('175), in view of the lack of an expectation of success, the teaching away found in the art of the time, and the unexpected results obtained in the present invention.

This discussion and the cited references provide substantial evidence that one of ordinary skill in the art would not have expected at the priority date that a soybean plant could display acceptable tolerance to glyphosate and a glufosinate without a loss of yield or injury to the plant. The withdrawal of the rejection under 35 U.S.C. §103(a) is thus respectfully requested.

C. Obviousness-type Double Patenting

Claims 1, 2 and 4-10 are rejected based on the judicially created doctrine of obviousness-type double patenting, in view of **(a)** claims 1-12 of issued U.S. Patent 6,376,754, and **(b)** claims 1-9 of U.S. Patent 5,710,368. Applicants traverse these rejections.

(a) The instant application is a divisional of the '754 patent, which was Application No. 08/813,788. Claims 1-12 of the '754 patent are directed to "[a] soybean seed having genes for resistance to glyphosate and sulfonylurea herbicides, wherein said glyphosate gene is an EPSPS gene which confers tolerance to glyphosate, and said sulfonylurea gene is an ALS gene which confers tolerance to sulfonylurea." By contrast, the claims of the instant application are directed to "A soybean seed comprising transgenes conferring resistance to at least the herbicides glyphosate and glufosinate . . . ." The October 10, 2000 Office Action in the '788 application imposed a restriction requirement requiring the election from among groups that differed in the

herbicide(s) to which the claimed soybean seeds are resistant. The group selected for prosecution in that case was the group in which soybean seeds are resistant to glyphosate and sulfonylurea. The claims of the instant application are directed to a different restriction group, i.e., to soybean seeds resistant to glyphosate and glufosinate, which was unelected in the '788 application. Since the instant application is a divisional of the '788 application with claims in a different and patentably distinct restriction group, the '788 application cannot be cited against the current claims. See MPEP 804.01 and 35 U.S.C. 121. Withdrawal of this rejection is thus respectfully requested.

(b) Regarding the '368 patent, the Action asserts that "[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because the species of the claims of the issued patent render obvious the genus encompassed by the instant claim." The '368 patent is directed to "[a] soybean seed designated 924181339 deposited as ATCC Accession No. 97555." The '368 patent further describes that soybean seed as, *inter alia*, having tolerance to Roundup™ and containing the ALS gene for sulfonylurea tolerance.

Applicants disagree with the assertion in the Action that the instant claims are generic to the claims of the '368 patent. As discussed in MPEP 806.04(d), ". . . a generic claim should require no material element additional to those required by the species claims, and each of the species claims must require all the limitations of the generic claim." However, the claims of the instant application require an additional material element not required in the '368 patent, *i.e.*, a transgene conferring resistance to glufosinate. Additionally, the claims of the '368 patent do not require all the limitations of the claims of the instant application, since the '368 patent claims do not require a gene for glufosinate resistance. Thus, the instant claims are not generic to the claims of the '368 patent.

Applicants also note that the subject matter of the '368 patent is that of the restriction group selected in the '788 patent, *i.e.*, resistance to glyphosate and sulfonylureas. Since that subject matter was deemed patentably distinct to the subject matter of the instant claims in the '788 restriction requirement, the instant claims must be patentably distinct from the '368 claims.

Since the instant claims are not generic to the claims of the '368 patent, and since the subject matters of the instant claims and the '368 patent were determined to be patentably distinct in the restriction requirement in the prosecution of the '788 patent, Applicants assert that the instant claims are not obvious in light of the '368 patent claims, and respectfully request withdrawal of this rejection.

D. Conclusion

In view of the above, it is submitted that all of the rejections to the claims have been overcome, and the case is in condition for allowance.

The examiner is invited to contact the undersigned with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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